

Thermally Injured Patients Are at Significant Risk for Thromboembolic Complications

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Background: The incidence of thromboembolic complications such as deep vein thrombosis (DVT) and pulmonary embolism (PE) in thermally injured patients is considered sufficiently uncommon that routine prophylactic measures are not warranted. Nevertheless, the incidence of DVT/PE may be increasing.

Methods: The records of 1,300 patients admitted to our unit from January 1990 to June 1995 were reviewed.

Results: Twenty-three patients developed a clinically significant DVT, eight patients developed a PE, and two patients

developed both a DVT and a PE, for an overall DVT/PE incidence of 2.9%. Four of 10 PEs were felt to be fatal. The DVT/PE patients were older (mean age, 42.6 vs. 28.7; $p < 0.001$) and had larger burns (37% vs. 18%, $p < 0.001$) than patients without evidence of DVT/PE. Body weight appeared to also influence DVT/PE rates, with obese patients (>30% over ideal body weight) having a higher incidence than patients with low or normal body weight (7.2 vs. 2.7%, $p < 0.015$). Age and total body surface area (TBSA) burn had a synergistic effect on DVT/PE risk, with the

sum of age and TBSA burn exerting the strongest independent effect when discriminant function analysis was performed ($p < 0.001$).

Conclusion: One can identify a population at increased risk of DVT/PE on the basis of the sum of age and TBSA burn, but prospective screening trials that assess all risk factors for DVT/PE should be performed before routine prophylaxis is used in thermally injured patients.

Key Words: Thermal injury, Deep vein thrombosis, Pulmonary embolism, Thromboembolic.

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Thromboembolic risk in the general surgical population not receiving prophylactic treatment increases as the number of risk factors increases. Factors that place patients at increased risk are age over 40 years, obesity, a history of deep vein thrombosis (DVT) and pulmonary embolism (PE), estrogen therapy, duration of operation greater than 60 minutes, extensive soft tissue injury or fractures, operations such as hip or knee arthroplasty, and prolonged bed rest. Without prophylaxis, high-risk patients are likely to develop a calf vein DVT, have a 10% to 20% chance of developing a popliteal or proximal DVT, and have a 5% to 10% risk of a PE.¹ Trauma patients appear to fall into the high-risk category for thromboembolic complications, with an overall DVT rate of 58%, and an 18% incidence of proximal DVT, when they do not receive prophylaxis.² Ther-

mally injured patients, conversely, are believed to vary from the general trauma population in that they have a low incidence of DVT and PE. In large clinical series of thermally injured patients who did not receive prophylaxis, DVT occurred in 0.9% of patients and PE occurred in 0.4% to 1.2%.^{3,4} An apparent increased incidence of DVT/PE in our burn center prompted us to reexamine thromboembolic risk in our thermally injured patients.

MATERIALS AND METHODS

We reviewed the records of all 1,300 thermally injured patients admitted to the U.S. Army Institute of Surgical Research from January 1990 to June 1995. Patients with exfoliative conditions or necrotizing fasciitis were excluded. Clinical data collected on each patient included age, total body surface area burned, height and weight, history of previous DVT/PE, the occurrence of DVT or PE, and survival. Burn distribution was not obtained as part of this study. The diagnosis of DVT was made by either venography or duplex ultrasound, and the diagnosis of PE was made by clinical presentation, ventilation-perfusion lung scan, pulmonary angiogram, and/or autopsy. Height and weight measurements were available for 678 of the 1,300 patients and allowed us to calculate ideal body weight (IBW) by standardized tables. The retrospective nature of this study did not allow determination of such data as days of bed rest and days in splints. There were no routine prophylactic measures for DVT used during this study; however, vena caval filters were used in a majority of morbidly obese patients (>100 lb over IBW or >100% over IBW) as prophylaxis against pulmonary emboli.⁵

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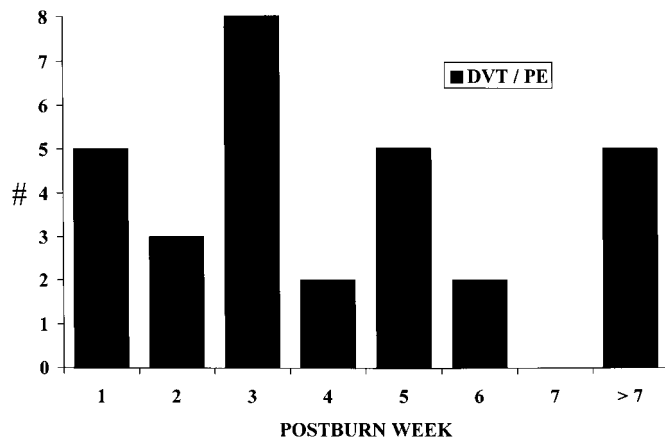


Fig. 1. The number of patients who had a DVT or PE detected each week are plotted as the y-axis and postburn week on the x-axis. A majority of thromboembolic events occurred in the first 5 weeks after burn, with an average postburn day for DVT/PE of 19.

For the purposes of this analysis, we did not determine a separate DVT and PE risk, but considered DVT and PE part of the same pathologic process. Collected data were examined by Student's *t* test or χ^2 analysis, as appropriate, to determine any association with DVT/PE. Factors found to be associated with increased incidence of DVT/PE were subjected to multivariate analysis by discriminant function analysis (STATISTICA for Windows 5.1, StatSoft, Inc., Tulsa, OK).

RESULTS

During this period, 31 of 1,300 (2.38%) thermally injured patients developed a thromboembolic complication. Twenty-one patients developed a clinically significant DVT, eight patients developed a PE, and two patients developed both a DVT and a PE, for an overall incidence of DVT and PE of 1.77% and 0.77%, respectively. Four of the 10 PEs were thought to contribute to or be a primary cause of death. The majority of thromboembolic events were detected in the first 5 weeks after burn, with an average postburn day of 19, and a range of 2 to 270 days (Fig. 1).

Patients who developed a thromboembolic complication were significantly older (42.6 vs. 28.7 years, $p < 0.001$) and had significantly larger burns (37.2 vs. 17.9%, $p < 0.001$) than those patients who did not develop DVT/PE (Table 1 and Fig. 2). In the cohort of patients with a thromboembolic event, patients over 50 years of age tended to have a less extensive thermal injury than patients under 50 years of age

Table 1 Risk Factors for DVT/PE

	DVT/PE (+)	DVT/PE (-)	p Value
Age, y	42.6 \pm 26.1	28.7 \pm 20.1	<0.001
TBSA, %	37.2 \pm 27.2	17.9 \pm 20.0	<0.001
IBW, %	126.2 \pm 32.0	113.8 \pm 24.2	0.015

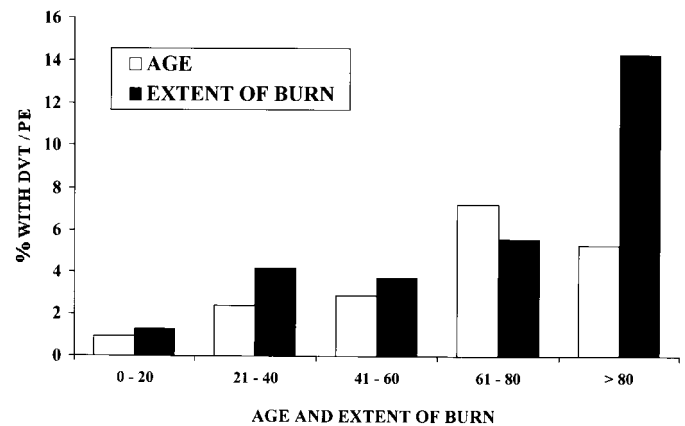


Fig. 2. The sum of age (years) and extent of burn (percent of body surface) are grouped by 20 on the x-axis and the percentage of that group who developed a DVT or PE on the y-axis. Both increasing age and extent of burn increase the risk for DVT and PE.

(Table 2). This trend did not attain statistical significance, but it did lead us to evaluate the sum of age and burn size as a separate risk factor for DVT/PE. The sum of these factors showed significant association with rates of DVT/PE (Fig. 3). For those patients for whom height and weight data were available (67% of 1,300 patients in the study), increased obesity (as measured by actual body weight as a percentage

Table 2 Extent of Burn (% TBSA) in Patients with DVT/PE

	TBSA		TBSA
Age < 40	40.5%	Age < 50	44.4%
Age \geq 40	33.2%	Age \geq 50	25.8%
p Value	0.468		0.063

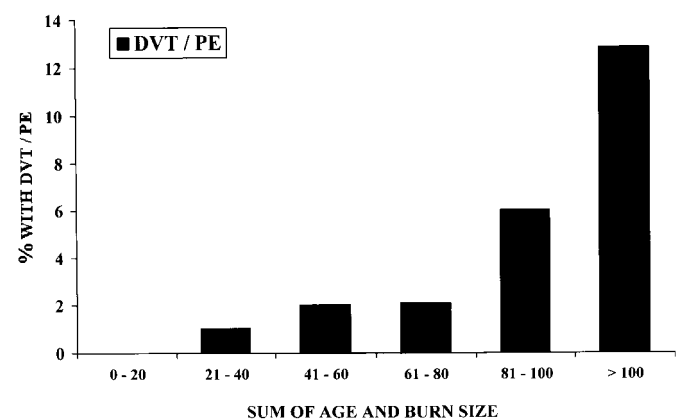


Fig. 3. The sum of age (years) and extent of burn (percent of body surface) is grouped by 20 on the x-axis and the percent of that group who developed a thromboembolic complication on the y-axis. There is an increasing incidence of DVT/PE with increasing "age + burn size." This trend is highly significant ($p < 0.001$). The most dramatic cut-point occurs at a sum of age and burn size greater than 80.

of ideal body weight) correlated with higher rates of DVT/PE (Table 1). Examining body weight at defined cut-points such as obesity (>30% above IBW) and morbid obesity (>100 lb or 100% above IBW) showed a consistent association of weight with thromboembolic risk. Nine of 126 obese patients suffered a DVT/PE, compared with only 15 of 552 nonobese patients experiencing this event (7.1% vs. 2.7%, $p = 0.015$). Morbid obesity was also a strong discriminator, with 4 of 27 morbidly obese patients experiencing a thromboembolic complication and only 20 of 651 nonmorbidly obese suffering a thromboembolic event (14.8% vs. 3.1%, $p = 0.001$). Two patients were noted to have a previous DVT/PE and six patients had a history of malignancy; one of these patients with a positive cancer history developed a thromboembolic complication. Although this DVT/PE rate (16.6%) was statistically higher than the rate (2.3%) in the patients without a history of malignancy ($p = 0.022$), the very low numbers of evaluable patients with history of malignancy make questionable any conclusions drawn from this difference.

Multivariate analysis was performed to determine the factors that exerted independent effects on the rate of DVT/PE. Factors associated with DVT/PE risk by univariate analysis—age, total body surface area burned, sum of age and burn size, percentage of desired body weight, and obesity—were subjected to forward stepwise discriminant function analysis. The sum of age and extent of burn was identified as the strongest predictor of DVT/PE ($p < 0.001$). If the sum of age and burn size was eliminated from the analysis, both total burn size ($p < 0.001$) and age ($p = 0.003$) were found to exert significant independent risk for DVT/PE. In the subgroup of adults with height and weight measurements available, morbid obesity, in addition to the sum of age and burn size, also exerted a significant independent effect ($p = 0.006$).

DISCUSSION

Dramatic improvements in burn care have increased the LD₅₀ (burn size associated with a 50% mortality) for a 21-year-old, thermally injured patient from 45% in 1950 to over 90% by 1990 in our and other burn centers.⁶ Resuscitative strategies, topical antimicrobials, early excision and grafting, nutritional support, and therapies directed at the sequelae of inhalation injury have improved survival and outcomes. Whereas further gains in survival rates may be possible, especially in high-risk populations such as the elderly, increasing attention has been paid to reducing the morbidities and long hospital stays associated with thermal injury. Preservation of lean body mass by hormonal manipulation and reduction of hypertrophic scarring by the development and use of composite artificial skins and dermal substitutes are areas of intense research. Reduction of thromboembolic events should improve survival by reducing fatal PE and should decrease morbidity by eliminating the need for treatment of acute DVT and the occurrence of the postphlebotic syndrome. The incidence of the postphlebotic syndrome has

not been evaluated in patients, but it may contribute to swelling or delayed wound healing of the lower extremities. It has long been argued that thromboembolic events are rare in thermally injured patients because the hyperdynamic circulatory state and increased blood flow to burned areas theoretically reduces venous stasis.⁷ Treatments directed at preventing DVT/PE, therefore, would have little benefit and significant risk. The purpose of this study was to reexamine the incidence of thromboembolic risk in thermally injured patients to possibly reassess the need for prophylactic DVT/PE treatment.

General surgical patients who do not receive prophylaxis may be grouped into low, moderate, and high risk for proximal vein DVT and have DVT rates of 0.4%, 2% to 8%, and 10% to 20%, respectively. Their rates of symptomatic PE are 0.2%, 1% to 8%, and 5% to 10%, respectively, with the high-risk group having a 1% to 5% risk of having a fatal PE.¹ Clearly, the moderate- to high-risk general surgical population need DVT/PE prophylaxis, which should reduce their risk by 30% to 50%. Trauma patients fall into the high-risk category for thromboembolic complications. In a prospective study of 349 trauma patients not receiving prophylaxis, Geerts et al.² showed an overall DVT rate of 58% by using ascending venography, with 18% of patients developing a proximal DVT. Although most studies have documented that 50% of DVT patients are asymptomatic, the study by Geerts et al. showed that nearly all were asymptomatic (98%). PE was diagnosed in 2% of patients and strongly suspected in an additional 3% of the study population. Three of seven documented PEs were fatal. Factors found to have predictive value of thromboembolic events (in ascending order) were age, surgery, femur or tibia fracture, and spinal cord injury.² Given the high rate of clinically silent DVT and the mortality associated with PE, Rogers et al.⁸ at the University of Vermont placed vena caval filters in patients felt to be at high risk for PE. They reported that the rate of PE in their institution fell by 75% because of this intervention.⁸

Thermally injured patients are believed to vary from the general trauma population in that they have a low reported incidence of DVT and PE.³ In their study of 1,439 adult burned patients, Purdue and Hunt³ found a negligible rate of PE. None of these PEs was thought to be fatal. Although burn size was not felt to be a risk factor, patients with PE had larger average burn size than that in the overall study burn population (26.8% vs. 18.6%). The authors concluded that the low risk of the condition did not justify routine prophylaxis in all patients, but that patients with severe leg burns, morbid obesity, or a history of prior DVT/PE should be given prophylaxis. Sheridan et al.⁵ at this center found a dramatically elevated incidence (>50%) of PE in the morbidly obese population. Three of four of these emboli were fatal and half occurred on heparin prophylaxis. This study prompted this burn center to use routine prophylactic vena caval filters in their morbidly obese patients. The most thorough analysis of DVT/PE risk in burn patients was performed by Rue et al.,

who reviewed 2,103 patients admitted to the U.S. Army Institute of Surgical Research from 1980 to 1989.⁴ A small number of patients received prophylaxis against thromboembolism during this period. Nineteen of 2,103 patients (0.9%) developed a clinically symptomatic DVT and 25 of 2,103 patients (1.2%) developed a PE. Three of the 25 PEs were felt to be the cause of death. Although trends existed for increased risk of DVT and PE with increasing age and extent of burn, log-linear analysis showed no statistically significant association. They concluded that, since heparin use increases the risk of bleeding and thrombocytopenia, prophylaxis with this agent should be limited to morbidly obese patients or patients with large burns that include the lower extremity.⁴

Our retrospective analysis, conducted in the same burn center for the 6 years after the study by Rue et al., showed an increased incidence of DVT, from 0.9% to 1.8% of admissions. This increase and the subsequent treatment for DVT may have been instrumental in reducing the rate of PE—from 1.2% to 0.8% of admissions—between the two study periods. The reason for the increased incidence of DVT and the overall thromboembolic complication rate found in this study may be multifactorial. Improvement in survival after thermal injury, which occurred over the 16-year period of the two studies, created a larger population at risk for DVT/PE. The possibility of observer bias in the form of heightened suspicion should also be considered as a possible cause and is borne out by the earlier mean postburn date of diagnosis, which decreased from 31 days to 19 days between the two periods. Also, the availability and accuracy of duplex ultrasound permitted easy and rapid determination of the presence of thrombosis and may have allowed for more frequent confirmation of clinical suspicion.

This study suggests that thermally injured patients are at increased risk for DVT/PE and that both advanced age and extent of burn increase this risk. In the study population with DVT/PE, older patients (>50 years) had smaller burn sizes than their younger counterparts. Age and burn size exerted a synergistic effect on thromboembolic risk, as shown by multivariate analysis, where each exerted an independent influence on DVT/PE risk. Combining age and burn size created the strongest risk factor for DVT/PE and allowed for the clearest graphic demonstration of this risk.

The findings of this study are consistent with the classic triad of Virchow. The effect of age may reflect the effect of stasis. Congestive heart failure, chronic venous insufficiency, and immobility associated with other conditions such as arthritis are more common with increasing age and can contribute to venous stasis. Extensive thermal injury, which has the strongest statistical power, appears to involve all of the Virchow triad. In this population, despite efforts at early, aggressive mobilization, the need for surgery requires a longer period of immobilization. These patients are hypercoagulable (other than during periods of infection) because of increased circulating clotting factors and platelets.⁹ Finally, patients with extensive injury more frequently undergo

scheduled laboratory analyses and central venous access, which can cause venous intimal damage and clot propagation.

Although this study identifies an at-risk group on the basis of the sum of age and burn size, this analysis was a retrospective review and should not be used to justify routine prophylaxis. Prophylaxis should reduce the incidence of DVT and, therefore, reduce the costs and morbidity of treatment for DVT and lead to a decreased incidence of postphlebotic syndrome, a potentially underrecognized complication after thermal injury. Unfortunately, treatment of established thrombosis with heparin or streptokinase does not appear to reliably change the rate of venous insufficiency, making the prevention of DVT the most appropriate management of this condition. In addition to reducing the morbidity of DVT, prophylaxis for DVT/PE may also improve survival by the reduction in fatal PEs. However, all of the potential benefits of prophylactic therapy must be reconciled with its risks. Even low-molecular-weight heparins are reported to be associated with major bleeding complications in up to 4% of treated patients.¹⁰ Antiplatelet antibodies occur in 1% to 5% of patients treated with unfractionated heparin and still occur, though at a lower rate, when fractionated heparins are used.^{10,11} In addition, the issue of cost must be considered with the routine use of these expensive medications. Inferior vena caval filters reduce the occurrence of PE, and therefore could be used as a prophylactic measure, but they are costly to insert and do not prevent the occurrence of deep vein thrombosis. A prospective evaluation of the occurrence of DVT/PE and the ability of prophylactic measures to reduce their occurrence with an acceptable rate of associated complications is warranted.

CONCLUSION

The sum of age and burn size, and the presence of morbid obesity, exert independent effects on the occurrence of thromboembolic complications after thermal injury. Of these factors, the sum of age and burn size is the strongest determinant for DVT/PE risk, with patients with a sum of these factors greater than 80 at considerable risk for thromboembolic events.

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